09/972,105 updated Search LYCOOK 5/3/06.

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(FILE 'HOME' ENTERED AT 09:06:09 ON 03 MAY 2006)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, JAPIO' ENTERED AT 09:06:45 ON 03
MAY 2006
1 152665 S (RED BLOOD CELL?)

L1L24120 S L1 AND FETAL? L32438 S L1 AND EMBRYO? L4718 S L2 AND L3 10 S L4 AND (PROTEIN EXPRESS?) L5 8 DUPLICATE REMOVE L5 (2 DUPLICATES REMOVED) L6 L7 17 S L4 AND REVIEW? L8 5 S L7 AND PROTEIN? L9 4 DUPLICATE REMOVE L8 (1 DUPLICATE REMOVED) L10 1 S L7 AND ISOLAT?

L11 101 S L4 AND ISOLAT? L12 77 DUPLICATE REMOVE L11 (24 DUPLICATES REMOVED)

L13 76 S L12 NOT L10

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ANSWER 4 OF 8 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN
     1999226588 EMBASE
AN
     Embryonic hemoglobins are expressed in definitive cells.
TΤ
ΑU
     Luo H.Y.; Liang X.L.; Frye C.; Wonio M.; Hankins G.D.V.; Chui D.H.K.;
     Alter B.P.
     Dr. B.P. Alter, Div. of Pediatric Hematology/Oncol., Children's Hospital,
CS
     University of Texas Medical Branch, 301 University Blvd, Galveston, TX
     77555-0361, United States. balter@utmb.edu
SO
     Blood, (1 Jul 1999) Vol. 94, No. 1, pp. 359-361. .
     Refs: 30
     ISSN: 0006-4971 CODEN: BLOOAW
CY
     United States
DT
     Journal; Article
FS
     025
            Hematology
LA
     English
SL
     English
ED
     Entered STN: 15 Jul 1999
     Last Updated on STN: 15 Jul 1999
AB
     Human embryonic \zeta and \epsilon globin chains are
     synthesized in yolk sac- derived primitive erythroid cells, and decrease
     rapidly during definitive erythropoiesis. Examination of and \epsilon
     globin expression at the cellular level using dual-color
     immunofluorescence staining with specific monoclonal antibodies showed
     that embryonic globin proteins are present in definitive
     erythroid cells. More than half of fetal erythrocytes were
     positive for \zeta and .apprx.5% for \varepsilon globin. Approximately one
     third of newborn red blood cells were
     ζ-positive and less than 1% ε-positive. Adult erythrocytes
     did not have embryonic globins. Erythroblasts that developed in
     liquid cultures also contained embryonic globin in amounts which
     declined with ontogenic age, and the proportion of positive cells in vitro
     was less than in the comparable erythrocytes that developed in vivo.
     Thus, embryonic globin chains are synthesized in definitive
     erythroid cells and decrease with ontogeny. Modulation of
     embryonic globin gene expression is not solely due to a switch
     from primitive to definitive erythropoiesis.
     Medical Descriptors:
     *hemoglobin determination
     *protein synthesis
     *erythropoiesis
     protein localization
     yolk sac
     erythroblast
       protein expression
     human
     article
     priority journal
     Drug Descriptors:
     *hemoglobin: EC, endogenous compound
     (hemoglobin) 9008-02-0
RN
```

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ANSWER 4 OF 8 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN
AN
     1999226588 EMBASE
     Embryonic hemoglobins are expressed in definitive cells.
TΙ
     Luo H.Y.; Liang X.L.; Frye C.; Wonio M.; Hankins G.D.V.; Chui D.H.K.;
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     University of Texas Medical Branch, 301 University Blvd, Galveston, TX
     77555-0361, United States. balter@utmb.edu
     Blood, (1 Jul 1999) Vol. 94, No. 1, pp. 359-361. .
     ISSN: 0006-4971 CODEN: BLOOAW
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     Journal; Article
             Hematology
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AB
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     that embryonic globin proteins are present in definitive
     erythroid cells. More than half of fetal erythrocytes were
     positive for \zeta and .apprx.5% for \epsilon globin. Approximately one
     third of newborn red blood cells were
     \zeta-positive and less than 1% \epsilon-positive. Adult erythrocytes
     did not have embryonic globins. Erythroblasts that developed in
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     declined with ontogenic age, and the proportion of positive cells in vitro
     was less than in the comparable erythrocytes that developed in vivo.
     Thus, embryonic globin chains are synthesized in definitive
     erythroid cells and decrease with ontogeny. Modulation of
     embryonic globin gene expression is not solely due to a switch
     from primitive to definitive erythropoiesis.
     Medical Descriptors:
     *hemoglobin determination
     *protein synthesis
     *erythropoiesis
     protein localization
     yolk sac
     erythroblast
       protein expression
     human
     article
     priority journal
     Drug Descriptors:
     *hemoglobin: EC, endogenous compound
RN
     (hemoglobin) 9008-02-0
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ANSWER 62 OF 76 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN
AN
     95313549 EMBASE
DN
     1995313549
TI
     Isolating fetal nucleated red blood
     cells from maternal blood: The Baylor experience - 1995.
     Simpson J.L.; Lewis D.E.; Bischoff F.Z.; Elias S.
ΑU
     Department of Obstetrics/Gynecology, Baylor College of Medicine, 6550
CS
     Fannin Ste. 701, Houston, TX 77030, United States
     Prenatal Diagnosis, (1995) Vol. 15, No. 10, pp. 907-912. .
SO
     ISSN: 0197-3851 CODEN: PRDIDM
CY
     United Kingdom
DT
     Journal; Conference Article
FS
             Obstetrics and Gynecology
     022
             Human Genetics
     025
             Hematology
LΑ
     English
SL
     English
ED
     Entered STN: 21 Nov 1995
     Last Updated on STN: 21 Nov 1995
AB
     In our previous work we have isolated fetal cells from
     maternal blood and used fluorescent in situ hybridization (F ISH) for
     chromosome-specific probes to detect aneuploidy. Current efforts in the
     Baylor College of Medicine programme are focusing on obtaining consistency
     in flow-sorting methodology and on determining sensitivity and
     specificity. To this end, systematic evaluation of five glycophorin A
     (gly A) antibodies all produced agglutination, leading us to abandon the
     use of gly A antibodies for positive selection of fetal cells.
     Conversely, we have found LDS-751 to be useful for nuclear selection.
     CD45 negative selection can best be accomplished by the use of flasks
     coated with goat antibodies against mouse antibodies. Positive selection
     by flow sorting for either CD71+ cells or gamma-globin-positive cells
     seems to be successful. Using these two approaches, we have recently
     detected male (fetal) cells in pregnancies in which the fetus
     was 46,XY in 10 of 18 and in 12 of 14 cases, respectively.
     Medical Descriptors:
     *aneuploidy
     *cell selection
     *fetus cell
     *maternal blood
     *prenatal diagnosis
     cell sorter
     conference paper
       embryo
     female
     flow cytometry
     fluorescence in situ hybridization
     human cell
     priority journal
     technique
     Drug Descriptors:
     *gamma globin
     *qlycophorin a
RN
     (glycophorin a) 112972-83-5
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ANSWER 62 OF 76 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN
     95313549 EMBASE
AN
DN
     1995313549
     Isolating fetal nucleated red blood
TТ
     cells from maternal blood: The Baylor experience - 1995.
     Simpson J.L.; Lewis D.E.; Bischoff F.Z.; Elias S.
AU
     Department of Obstetrics/Gynecology, Baylor College of Medicine, 6550
CS
     Fannin Ste. 701, Houston, TX 77030, United States
so
     Prenatal Diagnosis, (1995) Vol. 15, No. 10, pp. 907-912. .
     ISSN: 0197-3851 CODEN: PRDIDM
CY
     United Kingdom
DT
     Journal; Conference Article
             Obstetrics and Gynecology
FS
     010
     022
             Human Genetics
     025
             Hematology
LA
     English
SL
     English
ED
     Entered STN: 21 Nov 1995
     Last Updated on STN: 21 Nov 1995
     In our previous work we have isolated fetal cells from
AB
     maternal blood and used fluorescent in situ hybridization (F ISH) for
     chromosome-specific probes to detect aneuploidy. Current efforts in the
     Baylor College of Medicine programme are focusing on obtaining consistency
     in flow-sorting methodology and on determining sensitivity and
     specificity. To this end, systematic evaluation of five glycophorin A
     (gly A) antibodies all produced agglutination, leading us to abandon the
     use of gly A antibodies for positive selection of fetal cells.
     Conversely, we have found LDS-751 to be useful for nuclear selection.
     CD45 negative selection can best be accomplished by the use of flasks
     coated with goat antibodies against mouse antibodies. Positive selection
     by flow sorting for either CD71+ cells or gamma-globin-positive cells
     seems to be successful. Using these two approaches, we have recently
     detected male (fetal) cells in pregnancies in which the fetus
     was 46,XY in 10 of 18 and in 12 of 14 cases, respectively.
CT
     Medical Descriptors:
     *aneuploidy
     *cell selection
     *fetus cell
     *maternal blood
     *prenatal diagnosis
     cell sorter
     conference paper
       embryo
     female
     flow cytometry
     fluorescence in situ hybridization
     human
     human cell
     priority journal
     technique
     Drug Descriptors:
     *gamma globin
     *glycophorin a
RN
     (glycophorin a) 112972-83-5
```

ANSWER 46 OF 76 CAPLUS COPYRIGHT 2006 ACS on STN

- AN 1999:593845 CAPLUS
- DN 131:298449
- ED Entered STN: 21 Sep 1999
- TI Development, characterization, and use of monoclonal antibodies made to antigens expressed on the surface of **fetal** nucleated **red blood cells**
- AU Alvarez, Francisco V.; Olander, Jitka; Crimmins, Dan; Prieto, Belen; Paz, Ana; Alonso, Rebeca; Porter, Sharon; Hess, Jay; Crist, Robert D.; Landt, Yvonne; Ladenson, Jack H.
- CS Servicio de Analisis Clinicos, Hospital San Agustin, Asturias, 33400, Spain
- SO Clinical Chemistry (Washington, D. C.) (1999), 45(9), 1614-1620 CODEN: CLCHAU; ISSN: 0009-9147
- PB American Association for Clinical Chemistry
- DT Journal
- LA English
- CC 15-3 (Immunochemistry)
 Section cross-reference(s): 9, 14
- AB Background: Current methods for obtaining fetal cells for prenatal diagnosis are invasive and carry a small (0.5-1.0%) but definite risk of miscarriage. An attractive alternative would be isolation of fetal cells from peripheral maternal blood using antibodies with high specificity and avidity. Methods: To generate antibodies, we purified nucleated red blood cells (NRBCs) from fetal livers and used them as the immunogen to generate monoclonal antibodies (mAbs) directed against surface antigens. Results: The four antibodies recognized at least two conformationally sensitive epitopes of the transferrin receptor. Isolation of NRBCs from 252 maternal blood samples using these antibodies in magnetic activated cell sorting after an initial d. gradient centrifugation yielded 0-419 NRBCs per 25 mL of maternal blood. One antibody, 2B7.4, not only isolated the highest number of NRBCs but also isolated these NRBCs in 78 consecutive maternal samples. Conclusion: Antibody 2B7.4 shows promise for the isolation of NRBCs from maternal blood and should allow studies concerning the source of these cells, fetal vs. maternal, and the factors controlling their prevalence.
- ST monoclonal antibody fetal erythrocyte antigen prenatal diagnosis
- IT Blood Epitopes

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ANSWER 41 OF 76 CAPLUS COPYRIGHT 2006 ACS on STN
     2001:176541 CAPLUS
ΑN
DN
     134:324945
ED
     Entered STN: 15 Mar 2001
TΤ
     Antibodies to human fetal erythroid cells from a nonimmune phage
     antibody library
     Huie, Michael A.; Cheung, Mei-Chi; Muench, Marcus O.; Becerril, Baltazar;
AII
     Kan, Yuet W.; Marks, James D.
     Department of Dermatology, University of California, San Francisco, CA,
CS
     94143, USA
     Proceedings of the National Academy of Sciences of the United States of
SO
     America (2001), 98(5), 2682-2687
     CODEN: PNASA6; ISSN: 0027-8424
PB
     National Academy of Sciences
     Journal
DT
     English
LA
     15-3 (Immunochemistry)
CC
AΒ
     The ability to isolate fetal nucleated red
     blood cells (NRBCs) from the maternal circulation makes
     possible prenatal genetic anal. without the need for diagnostic procedures
     that are invasive for the fetus. Such isolation requires
     antibodies specific to fetal NRBCs. To generate a panel of
     antibodies to antigens present on fetal NRBCs, a new type of
     nonimmune phage antibody library was generated in which multiple copies of
     antibody fragments are displayed on each phage. Antibody fragments
     specific for fetal NRBCs were isolated by extensive
     predepletion of the phage library on adult RBCs and white blood cells
     (WBCs) followed by pos. selection and amplification on fetal
     liver erythroid cells. After two rounds of selection, 44% of the
     antibodies analyzed bound fetal NRBCs, with two-thirds of these
     showing no binding of WBCs. DNA fingerprint anal. revealed the presence
     of at least 16 unique antibodies. Antibody specificity was confirmed by
     flow cytometry, immunohistochem., and immunofluorescence of total
     fetal liver and adult RBCs and WBCs. Antibody profiling suggested
     the generation of antibodies to previously unknown fetal RBC
     antigens. We conclude that multivalent display of antibodies on phage
     leads to efficient selection of panels of specific antibodies to cell
     surface antigens. The antibodies generated to fetal RBC
     antigens may have clin. utility for isolating fetal
     NRBCs from maternal circulation for noninvasive prenatal genetic
     diagnosis. Some of the antibodies may also have possible therapeutic
     utility for erythroleukemia.
ST
     antibody selection phage display fetus erythroid cell antigen
IT
     Hematopoietic precursor cell
        (erythroid; selection of antibodies to human fetal erythroid
        cells from a nonimmune phage antibody library)
ΙT
        (erythroleukemia; selection of antibodies to human fetal
        erythroid cells from a nonimmune phage antibody library in relation to)
     Embryo, animal
IT
        (fetus; selection of antibodies to human fetal erythroid
        cells from a nonimmune phage antibody library)
IT
    Antibodies
     RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP
        (monoclonal; selection of antibodies to human fetal erythroid
        cells from a nonimmune phage antibody library)
IT
     Erythrocyte
     Phage display library
        (selection of antibodies to human fetal erythroid cells from
       a nonimmune phage antibody library)
IT
    Antigens
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
```

(selection of antibodies to human fetal erythroid cells from

a nonimmune phage antibody library)

IT Antibodies

RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)

(single chain, Fv fragment; selection of antibodies to human **fetal** erythroid cells from a nonimmune phage antibody library in relation to)

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

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- (2) Andersen, P; Proc Natl Acad Sci USA 1996, V93, P1820 CAPLUS
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- (27) Zheng, Y; Hum Genet 1997, V100, P35 CAPLUS
- (28) Zipursky, A; Lancet 1959, Vi, P451

a nonimmune phage antibody library)

IT Antibodies

RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)

(single chain, Fv fragment; selection of antibodies to human **fetal** erythroid cells from a nonimmune phage antibody library in relation to)

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Adinolfi, M; Nat Genet 1992, V1, P316 CAPLUS
- (2) Andersen, P; Proc Natl Acad Sci USA 1996, V93, P1820 CAPLUS
- (3) Barcena, A; Exp Hematol 1999, V27, P1428 CAPLUS
- (4) Becerril, B; Biochem Biophys Res Commun 1999, V255, P386 CAPLUS
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- (9) de Kruif, J; Proc Natl Acad Sci USA 1995, V92, P3938 CAPLUS
- (10) Griffiths, A; EMBO J 1993, V12, P725 CAPLUS
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- (17) Pereira, S; J Immunol Methods 1997, V203, P11 CAPLUS
- (18) Poul, M; J Mol Biol 1999, V288, P203 CAPLUS
- (19) Schroder, J; J Med Genet 1975, V12, P230 MEDLINE
- (20) Sheets, M; Proc Natl Acad Sci USA 1998, V95, P6157 CAPLUS
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- (24) Vaughan, T; Nat Biotech 1996, V14, P309 CAPLUS
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- (27) Zheng, Y; Hum Genet 1997, V100, P35 CAPLUS
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ANSWER 24 OF 76 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
     STN
AN
     1997:107649 BIOSIS
DN
     PREV199799406852
     Specific approaches to fetal cells isolation from
TI
     maternal blood: Introduction.
AU
     Leschot, N. J.
CS
     Dep. Hum. Genetics, Academic Med. Cent., Univ. Amsterdam, P.O. Box 22700,
     1100 DE Amsterdam, Netherlands
     Early Human Development, (1997) Vol. 47, No. SUPPL., pp. S69-S72.
SO
     CODEN: EHDEDN. ISSN: 0378-3782.
DT
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     English
LA
ED
     Entered STN: 10 Mar 1997
     Last Updated on STN: 10 Mar 1997
CC
     Cytology - Human
                        02508
     Genetics - Human
                        03508
     Pathology - Diagnostic
                              12504
     Blood - Blood and lymph studies
                                       15002
     Blood - Blood cell studies
                                 15004
     Development and Embryology - General and descriptive
                                                             25502
     Development and Embryology - Morphogenesis
     Major Concepts
IT
        Blood and Lymphatics (Transport and Circulation); Cell Biology;
        Development; Genetics; Pathology
     Miscellaneous Descriptors
IT
        AMNIOCENTESIS; ANALYTICAL METHOD; BLOOD; BLOOD AND LYMPHATICS;
        CHORIONIC VILLUS SAMPLING; EMBRYONIC STRUCTURE; ERYTHROBLAST;
        FETAL; FETAL CELL ISOLATION; FETUS; GENETIC
        DIAGNOSIS; MATERNAL; MEDICAL GENETICS; NUCLEATED RED
        BLOOD CELL; OBSTETRICS; PRENATAL DIAGNOSIS; PRENATAL
        DIAGNOSTIC METHOD; SPECIFIC APPROACHES; TROPHOBLAST
ORGN Classifier
                    86215
        Hominidae
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
        human
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
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L13

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(FILE 'HOME' ENTERED AT 09:06:09 ON 03 MAY 2006)

76 S L12 NOT L10

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, JAPIO' ENTERED AT 09:06:45 ON 03 MAY 2006

	LIMI	2000	
L1		152665	S (RED BLOOD CELL?)
L2		4120	S L1 AND FETAL?
L3		2438	S L1 AND EMBRYO?
L4		718	S L2 AND L3
L5		10	S L4 AND (PROTEIN EXPRESS?)
L6		8	DUPLICATE REMOVE L5 (2 DUPLICATES REMOVED)
L7		17	S L4 AND REVIEW?
L8		5	S L7 AND PROTEIN?
L9		4	DUPLICATE REMOVE L8 (1 DUPLICATE REMOVED)
L10		1	S L7 AND ISOLAT?
L11		101	S L4 AND ISOLAT?
L12		77	DUPLICATE REMOVE L11 (24 DUPLICATES REMOVED)

09/972,105 Updated Search Ucook 5/3/06.

(FILE 'HOME' ENTERED AT 14:40:42 ON 03 MAY 2006)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, JAPIO' ENTERED AT 14:40:59 ON 03 MAY 2006 303 S (THROMBOSPONDIN RECEPTOR) L1 18 S L1 AND REVIEW? L2 L3 14 DUPLICATE REMOVE L2 (4 DUPLICATES REMOVED) 83711 S (HORMONE RECEPTOR) L4 24761 S (LIPOPROTEIN RECEPTOR) L5 L6 39530 S (P GLYCOPROTEIN) 6 S L4 AND L1 L7 L8 4 DUPLICATE REMOVE L7 (2 DUPLICATES REMOVED) L9 7 S L5 AND L1 5 DUPLICATE REMOVE L9 (2 DUPLICATES REMOVED) L10 L11 1 S L6 AND L1 1 S L11 AND L10 L12 1 S L12 AND L8 L13 L14 5556 S (GLYCOPHORIN A) L15 189 S L14 AND REVIEW? L16 1 S L15 AND L4 L17 0 S L15 AND L5 L18 0 S L15 AND L6 L19 189 S L14 AND REVIEW? 141 DUPLICATE REMOVE L19 (48 DUPLICATES REMOVED) L20 L21 3120 S L6 AND REVIEW? L22 1626940 S HORMONE? L23 128026 S L22 AND REVIEW L24 46 S L23 AND THROMBOSPONDIN? L25 39 DUPLICATE REMOVE L24 (7 DUPLICATES REMOVED) L26 1577 S L23 AND GLYCOPROTEIN 2 S L26 AND L14 L27

2 DUPLICATE REMOVE L27 (0 DUPLICATES REMOVED)

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L28